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LETTER TO THE EDITORS

Introduction

Repace and Lowrey (1985) estimate exposure to environmental tobacco smoke (ETS) in Appendix A. In Appendix B they extrapolate an exponential dose response curve to the number of lung cancer deaths presumed to be caused by passive smoking in the community. In Appendix C they contrast lung cancer mortality in nonsmokers, comparing Seventh Day Adventists (SDAs) with a group of non-SDAs and then, assuming this difference to be caused solely by passive smoking, extrapolate the putative effect of passive smoking to the U.S. population to estimate the decrease in life expectancy presumed to be due to ETS.

In the following, I express the difficulties I have in accepting these estimates.

Appendix A

With regard to environmental tobacco smoke, I question whether "the daily exposure of individuals can be estimated" accuratedly using global statistics as described in appendix A. By definition, exposure occurs to a nonsmoker in the presence of an active smoker. Couples or groups containing at least one nonsmoker and one person smoking are the appropriate statistical units, not the individual! Such groups are dynamic, especially at the worksite. In general, smokers mix with smokers and nonsmokers with nonsmokers. Thus, office workers often control their own microenvironment. Likewise, at home, couples tend to be or to become alike in their smoking behavior. Consequently, it is quite difficult to estimate the typical nonsmoker's exposure to ETS accurately. It can be shown that the estimates given in this paper are overestimates, caused by the authors' disregard of the grouping of smokers and nonsmokers.

Consider, for example, the derivation of exposure in the home (exposure at the worksite is much more dynamic and variable from site to site). In Appendix A2 Repace and Lowrey consider adult couples in which the husband works and in which 42% of the wives are also employed. From their sources, only 37% of these couples have a nonsmoker exposed to ETS. Assuming that exposure requires contemporaneous occupation of the same space, it follows that these couples are together, at most, 34% of the waking day (the time given for the husband to be at home). Irrespective of which partner smokes the 32 cigarettes per day (cpd) assumed for a typical smoker, the nonsmoker is exposed at home to, *at most*, $32 \times 0.34 = 11$ cpd and this occurs in 37% of all two-person homes. Repace and Lowrey estimate the exposure to be 22 cpd in 62% of homes!

Now, consider Appendix A1 in which the exposure at the worksite is estimated. At no point in their argument do the authors consider the aggregation of smokers with smokers and nonsmokers with nonsmokers. Instead they assume a perfect mixing of smokers and nonsmokers in deriving their estimates. If, on the other hand, all smokers worked with smokers and nonsmokers with nonsmokers, then the global statistics they use would still describe the population but there would be zero exposure to ETS! Repace and Lowrey's estimates can only therefore be taken as an upper boundary to the upper limit of exposure to ETS.

Their method of estimation may also be criticised on theoretical grounds. Here and elsewhere in the paper the authors multiply averages and assume that the resultant product is the average of the convolution of the two original statistical distributions. This is true only if the two variates are independent. If not, then

$$E(xy) = E(x) \cdot E(y) + \rho\sigma_x\sigma_y,$$

where ρ is the correlation coefficient of x and y, σ is the standard deviation, and E is the expectation or average. It is likely that the variate, air exchange rate, is positively correlated with both density of occupation and with respiration rate, and that duration of exposure is negatively correlated with density of occupation and with respiration rate. The combined effect of these associations are unknown.

Appendix B

In Appendix B, the model is given as

$$P(D) = 1 - \exp(bD),$$

where D is the exposure, b is a constant, and $P(D)$ is the risk of a lung cancer death. The use of this model may be criticised on the following grounds:

- the relationship of passive smoking with lung cancer has *not* been shown to be a cause and effect relationship so that such modelling is, at best, premature;
- "the assumption of a no-threshold effect for carcinogens is also unproved" (Abelson, 1984);
- "the ambient measurements may have little or no bearing on the amounts that actually reach the target tissue" (Doll, 1985).

Thus, it is unlikely that such a simple model will adequately describe a complex process of carcinogenesis. A more general approach recognizes that tumor response is a function of delivered dose, D^* and that D^* is a *nonlinear* function of D, the exposure. Thus, the one-hit model

$$P = 1 - \exp(-[a + bD])$$

is a special case of this relationship (Hoel *et al.*, 1983) where D has been substituted for D^*. Hoel *et al.* (1983) give scenarios in which the 'standard approach,' extrapolated below the range of observed values underestimates the dose required for a given tumor incidence by factors of 50 to 100. The "hockey stick" relationship for carcinogens whose metabolites form DNA adducts can easily be taken for a straight line relationship if the minimum observed exposure is above the curve on the "hockey stick" (Hoel *et al.*, 1983). In a comparable situation to environmental tobacco smoke, the delivered dose/administered dose of formaldehyde in ambient air was shown to be significantly nonlinear (Casanova-Schmitz *et al.*, 1984). Starr and Buck (1984) show that four common dose-response models, the probit, logit, Weibull and multistage, all fitted the observed data on cancer risk from formaldehyde inhalation and could not therefore be discriminated among on the grounds of goodness of fit. Assuming that these models can be compared in fitting both administered and delivered dose curves, Starr and Buck (1984) show that, in all models the use of delivered dose gave lower estimates and lower upper confidence limits of cancer risk for a given low administered dose. More important, the range of the upper confidence limits increased among models as the administered dose fell.

In the above two studies the examples are based on animal exposures with zero tumors at zero dose. The one-hit model used by Repace and Lowery likewise has a zero intercept term. This is equivalent to assuming that the mortality rate of lung cancer is zero in the absence of ETS. Thus, yet again, Repace and Lowrey assume ETS to be the sole cause of lung cancer in the nonsmoker!

Appendix C

Here, Repace and Lowrey (1985) use unpublished data on lung cancer deaths (LCDs) in two groups of nonsmokers, followed roughly for the same period. If we accept that biases in ascertainment, classification and recording of LCDs are comparable in these two groups of SDAs and non-SDAs, then what? As before, Repace and Lowrey (1985) ascribe this difference solely to differences in exposure to environmental tobacco smoke (ETS). We are not, however, given the death rates from other causes of death in these two groups. If the death rates for motor vehicle accidents differ in the two groups, would Repace and Lowrey ascribe this difference likewise to differences in ETS? Again if mortality from cancer of the reproductive system is higher in SDA women than in non-SDA nonsmokers, would Repace and Lowrey assume that passive smoking had a protective effect?

In an editorial comment on a prospective study over a 20-yr period, the conclusion is questioned that eating fish is beneficial to health, although a lower mortality from heart disease is demonstrated. The editor points out that fish consumption may be associated with higher rates from other causes of death (Glomset, 1985). A similar problem exists with this method of estimation.

Conclusion

In some situations, a case can be made for reversing the usual definitions of the null and alternative hypotheses (Anderson and Hauck, 1983). This, however, is *not one of them*. The null hypothesis that passive smoking and lung cancer mortality are causally unrelated still stands. Until it is rejected, I consider it irresponsible to apply risk management techniques, even if they had been applied correctly.

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References

Abelson, P. H. (1984) Environmental risk management (editorial). *Science* 226, 4678, 1023.

Anderson, S. and Hauck, W. W. (1983) A new procedure for testing equivalence in comparative bioavailability and other clinical trials. *Comm. Stat. Theor. Meth.* 12, 2663–2692.

Casanova-Schmitz, M., Starr, T. B., and Heck, H. d'A (1984) Dif-

ferentiation between metabolic incorporation and covalent binding in the labeling of macromolecules in the rat nasal mucosa and bone marrow by inhaled [^{14}C] and [^{3}H] formaldehyde. *Toxicol. Appl. Pharmacol.* 76, 26–44.

Doll, R. (1985) Occupational cancer: A hazard for epidemiologists. *Int. J. Epidemiol.* 14, 22–31.

Glomset, J. A. (1985) Fish, fatty acids, and human health. *New Eng. J. Med.* 312, 1253–1254.

Hoel, D. G., Kaplan, N. L. and Anderson, M. W. (1983) Implication of nonlinear kinetics on risk estimation in carcinogens. *Science* 219, 1032–1047.

Repace, J. L. and Lowrey, A. H. (1985) A quantitative estimate of nonsmokers' lung cancer risk from passive smoking. *Environ. Int.* 11, 3–22.

Starr, T. B. and Buck, R. D. (1984) The importance of delivered dose in estimating low-dose cancer risk from inhalation exposure to formaldehyde. *Fund. Appl. Toxicol.* 4, 740–753.